

**Amendments to the Claims:**

This listing of claims replaces all prior versions, and listings, of claims in the application:

1. (Currently amended) A chimeric polypeptide, said chimeric polypeptide comprising:
  - a) a first domain ~~comprising~~ consisting essentially of an ~~an~~ third intracellular loop (i3 loop) or a fragment thereof ~~portion~~ of a G protein coupled receptor (GPCR), and
  - b) ~~at least~~ a second domain, attached to the first domain, wherein said second domain is a naturally or non-naturally occurring cell-penetrating, membrane-tethering hydrophobic moietywherein said first domain does not comprise a native extracellular portion of said GPCR and wherein said chimeric polypeptide binds to its cognate GPCR.
2. (currently amended) The chimeric polypeptide of claim 1, wherein said ~~second or more domains are~~ hydrophobic moiety is attached at ~~either one end, at both ends, or at an internal position~~ the N-terminal end, the C-terminal end, or both the N-terminal and C-terminal ends of said first domain.
3. (previously amended) The chimeric polypeptide of claim 1, wherein said hydrophobic moiety is a lipid.
4. (amended herein) The chimeric polypeptide of claim 3, wherein said hydrophobic moiety is selected from the group consisting of: capryloyl (C<sub>8</sub>); nonanoyl (C<sub>9</sub>); capryl (C<sub>10</sub>); undecanoyl (C<sub>11</sub>); lauroyl (C<sub>12</sub>); tridecanoyl (C<sub>13</sub>); myristoyl (C<sub>14</sub>); pentadecanoyl (C<sub>15</sub>); palmitoyl (C<sub>16</sub>); phtanoyl ((CH<sub>3</sub>)<sub>4</sub>); heptadecanoyl (C<sub>17</sub>); and stearyl (C<sub>18</sub>), ~~stearyl (C<sub>18</sub>), palmitoyl (C<sub>16</sub>), myristoyl (C<sub>14</sub>), lauryl (C<sub>12</sub>), capryl (C<sub>10</sub>), and capryloyl (C<sub>8</sub>)~~ wherein said hydrophobic moiety is attached to said chimeric polypeptide with amide bonds, sulfhydryls, amines, alcohols, phenolic groups, or carbon-carbon bonds.
5. Cancelled.
6. - 9. Cancelled.
10. <sup>5</sup> (currently amended) The chimeric polypeptide of claim ~~6~~ 1, where said ~~intracellular portion is~~ i3 loop or fragment thereof comprises at least 3 contiguous amino acid residues of the third intracellular loop.

APPLICANTS: Kuliopulos et al.

APPLICATION NUMBER: 09/841,091

11. <sup>6</sup> (currently amended) The chimeric polypeptide of claim 6 1, wherein said ~~intracellular portion is~~ 3 loop or fragment thereof comprises at least 5 contiguous amino acid residues of the third intracellular loop.
12. (canceled)
13. <sup>7</sup> (currently amended) The chimeric polypeptide of claim ~~12~~ 1, wherein said ~~intracellular portion is~~ 3 loop or fragment thereof comprises at least 7 contiguous amino acid residues of the third intracellular loop.
14. <sup>2</sup> (Currently amended) The chimeric polypeptide of claim 1, wherein said first domain comprises a protease-activated receptor (PAR) and said second domain comprises a lipid moiety.
15. Cancelled.
16. Cancelled.
17. Cancelled.
18. Cancelled.
19. <sup>9</sup> (amended herein) The chimeric polypeptide of claim 1, wherein the G-protein coupled receptor or fragment thereof, is selected from the group consisting of a luteinizing hormone receptor, a follicle stimulating hormone receptor, a thyroid stimulating hormone receptor, a calcitonin receptor, a glucagon receptor, a glucagon-like peptide 1 receptor (GLP-1), a metabotropic glutamate receptor, a parathyroid hormone receptor, a vasoactive intestinal peptide receptor, a secretin receptor, a growth hormone releasing factor (GRF) receptor, protease-activated receptors (PARs), cholecystokinin receptors, somatostatin receptors, melanocortin receptors, ADP receptors, adenosine receptors, thromboxane receptors, platelet activating factor receptor, adrenergic receptors, 5-HT receptors, CXCR4, CCR5, chemokine receptors, neuropeptide receptors, opioid receptors, ~~erythropoietin receptor, von Willebrand receptor,~~ parathyroid hormone (PTH) receptor, and vasoactive intestinal peptide (VIP) receptor, ~~and collagen receptors.~~
20. - 28. Cancelled.
29. <sup>10</sup> (Original) A pharmaceutical composition comprising the chimeric polypeptide of claim 1 and a pharmaceutically acceptable carrier.

APPLICANTS: Kuliopulos et al.

APPLICATION NUMBER: 09/841,091

30. Cancelled.

~~31.~~ <sup>11</sup> (Original) A kit comprising in one or more containers, the pharmaceutical composition of claim ~~28.~~ <sup>10</sup>

32.- 34. Cancelled.

~~35.~~ <sup>12</sup> (Previously added) The chimeric polypeptide of claim 1, wherein said G-protein coupled receptor is a mammalian G-protein coupled receptor.

~~36.~~ <sup>13</sup> (Previously added) The chimeric polypeptide of claim 4, wherein said hydrophobic moiety is palmitoyl.

~~37.~~ <sup>14</sup> (Previously added) The chimeric polypeptide of claim ~~19~~ <sup>1</sup>, wherein said G-protein coupled receptor is a protease-activated receptor (PAR).

~~38.~~ <sup>15</sup> (Previously added) The chimeric polypeptide of claim ~~37.~~ <sup>14</sup>, wherein the protease-activated receptor is selected from the group consisting of PAR1, PAR2, and PAR4.

~~39.~~ <sup>16</sup> (Previously added) The chimeric polypeptide of claim ~~12~~ <sup>1</sup>, wherein said ~~intracellular portion i3 loop or fragment thereof~~ comprises a sequence selected from the group consisting of SEQ ID NO: 1-16, 19-23, and 29.

~~40.~~ <sup>17</sup> (currently amended) The chimeric polypeptide of claim ~~12~~ <sup>1</sup>, wherein said ~~intracellular portion i3 loop or fragment thereof~~ comprises a sequence selected from the group consisting of SEQ ID NO: 1-10, and 23.

~~41.~~ <sup>18</sup> (Previously added) The chimeric polypeptide of claim 1, wherein the said G-protein coupled receptor is selected from the group consisting of CCKA, CCKB, SSTR2, and SubP receptors.

~~42.~~ <sup>19</sup> (Previously added) The chimeric polypeptide of claim 3, wherein said hydrophobic moiety is a steroid.

~~43.~~ <sup>20</sup> (currently amended) A chimeric polypeptide, said chimeric polypeptide comprising:

- a) a first domain comprising an ~~intracellular portion~~ isolated i3 loop or fragment thereof of a protease-activated receptor (PAR), and
- b) a second domain, attached to the first domain, wherein said second domain is palmitate.

- ~~44.~~21 (new) The chimeric polypeptide of claim 1, wherein said hydrophobic moiety is selected from the group consisting of a phospholipid, a steroid, a sphingosine, a ceramide, an octyl-glycine, a 2-cyclohexylalanine, and a benzoylphenylalanine.
- ~~45.~~22 (new) The chimeric polypeptide of claim 1, further comprising a third domain, said third domain being a cell-penetrating, membrane tethering hydrophobic moiety attached to said first domain.
- ~~46.~~23 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:1.
- ~~47.~~24 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:2.
- ~~48.~~25 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:3.
- ~~49.~~26 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:4.
- ~~50.~~27 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:5.
- ~~51.~~28 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:6.
- ~~52.~~29 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:7.
- ~~53.~~30 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:8.
- ~~54.~~31 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:9.
- ~~55.~~32 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:10.
- ~~56.~~33 (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:11.

APPLICANTS: Kuliopulos et al.

APPLICATION NUMBER: 09/841,091

- ~~57.~~<sup>34</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:12.
- ~~58.~~<sup>35</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:13.
- ~~59.~~<sup>36</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:14.
- ~~60.~~<sup>37</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:15.
- ~~61.~~<sup>38</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:16.
- ~~62.~~<sup>39</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:19.
- ~~63.~~<sup>40</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:20.
- ~~64.~~<sup>41</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:21.
- ~~65.~~<sup>42</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:22.
- ~~66.~~<sup>43</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:23.
- ~~67.~~<sup>44</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:28.
- ~~68.~~<sup>45</sup> (new) The chimeric polypeptide of claim 1, wherein said i3 loop or fragment thereof comprises the amino acid sequence of SEQ ID NO:29.
- ~~69.~~<sup>46</sup> (new) The chimeric polypeptide of claim 1, wherein the hydrophobic moiety is a steroid.